Chapter

Biomedical Applications of Silver Nanoparticles

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Abstract

Nanotechnology is a branch of science and engineering dedicated to materials, having dimensions in the order of nanometer scale and it has been widely used for the development of more efficient technology. Nanoparticles offer many benefits to bulk particles such as increased surface-to-volume ratio, and increased magnetic properties. In recent years, nanotechnology has been embraced by industrial sectors due to its applications in the field of electronic storage systems, biotechnology, magnetic separation and pre concentration of target analytes, targeted drug delivery, and vehicles for gene and drug delivery. Over the year's nanomaterials such as nanoparticles, nanoclusters, nanoreods, nanoshells, and nanocages have been continuously used and modified to enable their use as a diagnostic and therapeutic agent in biomedical applications. Thus, In this chapter, introduction to metal nanoparticles, synthesis (Chemical and green synthesis) and biomedical application silver nanoparticles are presented.

Keywords: Green Synthesis, Metal Nanoparticles , Silver nanoparticles , Biomedical Applications

1. Introduction

The trend of miniaturization combined with technological modernization requirements has led to the substantial rise in exploring nanoparticles. The discoveries of new antibiotics, conventional drugs and chemically modified drugs can not only resolve the microbial resistant issues but also necessitates a prolonged effective metallic nanotechnology in diverse applications. Nanomaterials such as nanoparticles, nanoclusters, nanorods, nanoshells, and nanocages are modified constantly to enable their use as a diagnostic and therapeutic agents applications. Theefficacy of the nanoparticle can be determined by its size, structure, concentration, dimensions and ionic strength accompanied with surface coating can support additional strength and durability as a carrier for a wide range of therapeutic components in several biomedical applications. Nanoparticles offer various benefits to bulk particles with increased surface-to-volume ratio, magnetictarget [1, 2], wound healing properties [3], biocomposite preparation, gene and drug delivery vehicles [1, 2, 4].

Nanoparticles synthesis and characterization have flourished due to their wide-ranging applicability particularly as catalysts in biomedical, optics, and energy fields [5]. Among the classified nanoparticles, metalnanoparticles have fascinated, due to their distinctive physical and chemical properties, selectivity, highly active, and reproducibility. Among different metal nanoparticles, silver nanoparticles (AgNPs) have attracted considerable researcher's attention because of its high electrical and thermal conductivity, surface-enhanced Raman scattering, chemical stability, catalytic activity and antimicrobial activity [6, 7]. Silver nanoparticles are increasingly being applied in biomedicines for their respective broad antimicrobial behavior becoming more attractive for use in drug delivery and targeting especially for their tunable hydrophilic - hydrophobic balance and target specific localization surface features as versatile opportunities in drug delivery and modification systems [6, 7]. The above mentioned properties have enabled silver nanoparticles to serve as a material in the development of new generation electronic, optical and sensor devices.

2. Synthesis of metal nanoparticles

In the synthesis of nano materials, particularly metallic nanoparticles, has raised greatest attention over the past decade due to their exclusiveproperty that make them suitable in various fields of science and technology. There is a scarcity of effective methods to synthesis a homogeneous size and shape nanoparticles with limited or no toxicity to the human health and the environment. There are two methods for the synthesis of metallic nanoparticles- top-down and bottom-up approaches [8]. In bottom-up approach, reduction of materials components with further self-assembly process which leads to the formation of nanostructures. Representative examples include Quantum dot and formation of nanoparticles from colloidal dispersion. In Top down approach [9] includes the macroscopic structures which can be externally controlled in the processing of nanostructures, such as ball milling, application of severe plastic deformation [10].

3. Chemical synthesis/green synthesis of metal nanoparticles

Even though nanoparticles can be made using various physicochemical methods their synthesis using nontoxic and environmentally kind biological methods is attractive specially. The biological method (green synthesis) is comparatively easy, economical, and environmentally affable method than the conventional chemical method of synthesis and thus accomplish an upper hand. Numerous studies have shown that characteristics of metallic nanoparticles such as size, stability, physical, chemical properties and morphology are strongly influenced by the experimental conditions. Several routes have been developed for biological or biogenic synthesis of nanoparticles from salts of the corresponding metals [11–14]. Microorganisms, whole plants, plant tissue and fruits, plant extracts and marine algae [15] have been used to synthesis nanoparticles.

Plants are regarded as a highly desirable system for nanoparticle synthesis due to their tremendous capability to produce a broad range of bioactive secondary metabolites with profound reducing potential. As compared to bacteria and algae and, plants are less vulnerable to metal toxicity, thus offering a green substitute for the biosynthesis of metal nanoparticles [16].

4. Green synthesis of silver nanoparticles using leaf, seed, fruit, bark and their potential

Among all metal nanoparticles, silver nanoparticles are of great significance in the field of nanotechnology [17]. Nanoparticles are synthesized by physical, chemical, and biological or green methods. Various chemical and physical methods are proved to be quite expensive and the use of various toxic chemicals that are responsible for various biological risks. This may be the reason for choosing biosynthesis of nanoparticles via green routethat does not employ toxic chemicals and proved to be eco-friendly [18]. Silver nanoparticles are the most prototypical target of green methods [19–23] and can be synthesized using plant extracts.Gold and silver metal nanoparticles weregreen synthesized using the Root Extract of Coleous forskohlii as capping and reducing agent for biomedical applications [24].

5. Biomedical application of silver nanoparticles

Silver nanoparticles have diverted the attention of the scientific community and industrialist itself due to their wide range of applications in industry for the preparation of consumer products and highly accepted application in biomedical fields. Silver has function in antimicrobial, catalytic and biological systems and the unique physical and chemical properties of silver nanoparticles only increase the efficacy of silver. Though there are many mechanisms ascribed to the antimicrobial activity shown by silver nanoparticles, the actual and most reliable mechanism is not fully understood or cannot be generalized as the nanoparticles are found to act on different organisms in different ways.

During the past few years, silver nanoparticles became one of the most examined and explored nanotechnology-derived nanostructures, given the fact that silver nanoparticles proved to have interesting, challenging, and promising characteristics suitable for various biomedical applications [25]. Even though there is limited information regarding the toxicity and in vivo biological behavior, these nanostructures were used for a long time as antibacterial agents in the health industry cosmetics, food storage, textile coatings and some environmental applications [26].

The exclusiveproperty of silver nanoparticles areparticularly advantageous for cancer therapeutics since they led to an improved chemotherapeutic efficiency together with minimal systemic toxicity [27]. AgNPs attracted special attention for this particular domain, and were successfully evaluated as effective anti-tumor drug-delivery systems [28], acting either as passive [29] or active [30] nanocarriers for anticancer drugs. Recent studies evidenced the potential use of AgNPs as vaccine and drug carriers for specific and selective cell or tissue targeting [31]. In addition tothe great optical properties of AgNPs [32–34] the recent improvements in AgNP biocompatibility and stability viasurface modification strongly recommend nanostructured systems based on silver as specific, selective,and versatile candidates for drug-delivery applications [35].

6. Silver nanoparticles as antimicrobial agents

Researches on the synthesis of silver nanoparticles using microbes and plant extract has become active due to its easy accessibility, non-toxicity, wide ranged applications, flexibility and essentially for its biodegradability, sustainability and cost effectivity. Various plants are being effectively used for the synthesis of metal nanoparticles. Various plant parts including fruit peels, leaves, barks, flowers, roots are used in synthesizing silver and other metal nanoparticles. Silver nanoparticles can serve as a medium for the delivery of antibiotics and disinfecting materials. Silver ions (Ag^+) and their respective compounds are highly toxic to broad spectral microorganisms. As a biological approach, different plants.

7. Antibacterial

Silver has been found in our traditional medicines and culinary for a long time. Silver is known to cause bacteriostatic (growth inhibition) and bactericidal (eradicate) properties, hence described as oligodynamic it is metals enclose ions that devastate living cells, like fungi, bacteria, and viruses. Silver in ionic forms strongly interacts with thiol groups of vital enzymes in bacteria and inactivates them and thereby making it lose their ability to replicate their DNA. Silver compounds such as silver nitrate and silver sulfadiazine are being used to prevent bacterial growth in sterilization process of drinking water and also in burn care activities. Silver nanoparticles has been widely used as antibacterial agents for centuries that exerts bactericidal activity even at minimal concentration which has lead its use against antibiotic resistant bacteria and prevents against a broad range of pathogenic microorganisms. Silver nanoparticles have been found to destabilize the membrane potential and deplete the intracellular ATP (Adenosine tri-phosphate) levels by target resulting in death of the bacteria.

8. Antifungal

Silver displays multiple mode of inhibitory mechanisms against microorganisms. Silver nanoparticles can be actively applied in the field of plant protection following the emergence of various resistant fungal pathogens leading to the reduction in agricultural production.The antifungal potential of silver nanoparticles was tested against various human pathogens, plant pathogens, wood degrading fungi including *Aspergillusochraceus*, *Candidaalbicans*. *Macrophominaphaseolina*, *Fusariumoxysporum*, *Fusariumsolani*, *Trichoderma* sp., and *Alternariaalternate* [36], *Raffaelea* sp., *Alternariabrassicicola*, *Botrytiscinerea*, *Cladosporiumcucumerinum*, *Corynesporacassiicola*, *Cylindrocarpondestructans*, *Didymellabryoniae*, *Glomeirellacingulata*, *Monosporascuscannonballus*, *Pythiumaphanidermatum*, *Pythiumspinosum*, *Stemphyliumlycopersici* [37] commercially important fungal pathogens were tested to check the fungicidal properties of silver nanoparticles. The findings suggest that silver nanoparticles are capable of inhibiting the above mentioned pathogens with slight variations according to the silver nanoparticles applied. Most of the fungi showcased higher inhibition rate at low concentrations of silver nanoparticles. Though very little is known about the effects of silver nanoparticles on phytopathogenic fungi, certain studies carried out proved the efficiency of silver nanoparticle on inhibition of mycelial growth and conidial germination.

9. Anticancer

Cancer cells have abnormal metabolic behaviors and genomic expressions by causing various pathological and metabolic alterations in cellular surroundings developed by cell signaling, rapid proliferation, angiogenesis and metastasis. Many studies reported depicts that the use of silver nanoparticles enhances the chemotherapeutic efficacy against multidrug resistant cancer cells emphasized with specifications and combinations. Nanoparticles coated with specific binders can recognize particular surface receptors and targets only the cancerous cells or the anomalous cells. Many platinum nanoparticles and platinum based compounds were approved as anticancer agents. Though many cancer types are susceptible to platinum based drugs accompanied with toxic side effects. Consequently other metal nanoparticles are explored in search of a better anticancer agents, while silver with advantageous antimicrobial activity arose into interest as an effective anticancer agent. Cancer cells such as HepG2 (human liver cancer cells) [24], HCT (Human colon cancer cells), HeLa (Human cervical adenocarcinoma cells), MCF 7 (Human breast adenocarcinoma cells) [24] and various other cancer cells were used to study the cytotoxicity effect of silver nanoparticles. Silver nanoparticles synthesized using different plant extracts showed potentially high cytotoxicity and less cell viability against various cancer cells. Moreover, nanoparticles of 5-35 nm sizes effectively induced cell death through mitochondrial structure targeting [38].

10. Silver nanoparticles for drug-delivery systems

Metallic nanoparticles had emerge as probable antimicrobial agents due to their ultra-small size, high surface to volume ratio, novel physiochemical properties rooted from interaction with microbes including cellular uptake and aggregation leading to toxicity and death of the microbe [39]. Ligand dependent silver release with drug may offer potent synergistic antimicrobial activities not only for drug but also for AgNPs due to their short carbon chain and weak binding atom of oxygen. Therefore, the optimization of the surface ligands such as coordination atoms, carbon chain lengths and terminal groups is very important to prepare nanoparticles for commercial applications against infectious diseases [40]. Research evidences shows that modification of silver nanoparticles could be exploited for drug delivery and are used to modulate the toxic actions of drugs. It also accompanies that as the concentration increases, non-significant reduction in the cytotoxic actions for the silver nanoparticle conjugates were relative to the cytotoxicity of the cells.

11. Silver nanoparticles for catheter modification

In generalmicrobes adhere on the surface of the catheters and growsrapidly forming biofilmsin such environmental conditions leading to bloodstream infections, even worse. Silver impregnated catheters have already been used in clinical fields and silver nanoparticles are applied in number of biomedical devices. Methods like solvent casting, electrospinning, electrospraying, and silver iontophoretic technology were being used for the synthesis of silver impregnated catheters. The nature of silver nanoparticles and the coating incorporation will determine the efficacy and durability of the medical devices.

12. Silver nanoparticles for dental applications

Silver has been proven to be less toxic and a good biocompatible with human cells [41]. Silver nanoparticles are used as endodontics, several areas of dentistry such as implantology, restorative dentistry and dental prostheses. Use of silver nanoparticles in dentistry is mainly to inhibit or decrease the growth of microbial colonization over the dental materials to improve and maintain oral health. Other advantage being the penetration possibility of silver nanoparticles through cell membranes resulting in higher antimicrobial activity especially for biofilm forming microbes. Silver nanoparticles incorporated in dental materials through distinct methods depending on the type of materials. For dental implants titanium samples are immersed in silver nitrate solution and irradiated with UV(Ultraviolet) light after wash and dried [42]. Whereas, for adhesive/resin composite a monomer preferably 2-tert-butylamino-ethyl-methacrylate is added to improve the silver solubility [43]. In order to improve quality and durability of polymeric restorative materials many studies are being performed. Rather than notable advancements, restoration composite materials accumulate more biofilms. Actually an imperfect sealing between the restoration composite material and the cavity wall leads to the colonization of oral microbes resulting in secondary caries leading to replacements. To avoid such complications, restorative materials with antimicrobial property has to be incorporated.

13. Silver nanoparticles for wound healing

The disruption of skin integrity defines the formation of a wound, which can be classified into acute (burns), chronic (diabetic foot) and pressure ulcers [44]. Due to the development of antibiotic resistant and outbreak of infectious diseases, the scientists are eyeing for better replacements. Indeed, there is rise in interest in silver nanoparticles integrated biopolymers in wound healing applications. A review conducted by Sim *et al*., on the silver based patented products revealed that over 5000 new applications were registered during 2007–2017 [45]. Silver based products are patented and commercialized for their improvised designs and efficacies than the standard dressing materials. The antimicrobial effect of silver significantly reduces the hazardous natureof microorganisms to develop resistance and increases the efficiency against multi-drug-resistant microbes.An active role of silver nanoparticles attributed in wound healing mechanisms along with its distinctive role in preventing infections, which in turn promotes faster healing rates, stimulated proliferation, relocation of keratinocytes and wound contraction [3]. The antimicrobial therapy which mainly supervise the process such as Colonization, proliferation of pathogens along with multidrug confrontation which serves as foremost and imperative aspects of skin and wound care. Enchantingly, silver and silver ions havebeen engaged for thousands of years since their bactericidal activity that include.Antibacterial effects at the multilevel approach that aims at reducing chances of enlargement of confrontation, and this purpose is served via blocking the respiratory enzymes. Efficiency against multi drug resistant organisms. Low systemic toxicity. A significant volume of research data has provided confirms the beneficial effects of silver nanoparticles as biocompatible, however, the interaction mechanism between silver nanoparticles and the microbial flora, along with clinical toxicity studies are still requires deep investigations. Medical products such as bandages, gauzes, sutures, plasters, textile materials, creams and ointments can be functionalizedwith silver nanoparticles for wound healing property. A synergistic effect between silver and silk protein sericin improved tissue regeneration and antimicrobial properties, a natural wound dressing biomaterial approved [46].

14. Silver nanoparticles for bone healing

Human bones are composed of crystallized hydroxyapatite, a form of calcium and phosphate. It is a widely accepted and used body implant material. As a suitable choice for the fabrication of antimicrobial and bioactive bone implants biocompatible hydroxyapatiteintegrated either with metallic or ionic silver forms are used as superficial implant materials. Such hydroxyapatite coatings embedded with silver nanoparticles found to be an effective inhibitors of both Gram positive and Gram negative bacteria [47]. In addition to antimicrobial property, the additive should provide additional optical, mechanical, chemical properties to achieve enhanced biomaterials Kora *et al*, [48].

15. Toxicity of silver nanoparticles

Over the years, silver nanoparticles have been subjected to numerous in vitro and in vivo tests to provide information about their toxic behavior towards living tissues and organisms. The biosafety of silver nanoparticles has gained much attention for its interaction with blood and tissues. Considering their unique physical and chemical properties, it is likely that these silver nanoparticles besides possess distinctive toxicity mechanisms, a better understanding of silver nanoparticles safety is essential, in order to escalate their clinical use [49]. It was proven that nanosilver can cause the formation and intracellular accumulation of ROS (Reactive Oxygen Species), modification of mitochondrial membrane permeability and DNA (Deoxyribo Nucleic Acid) damage. Variousscientific research proved that silver nanoparticles disclosure can induce a decrease in cell viability through different cellular mechanisms. One of these mechanisms is represented by the induction of apoptosis-related genes and the activation of apoptosis mechanism [50].

16. Conclusions

Silver nanoparticles are intensively explored nanostructures for exceptional and enhanced biomedical applications, thanks to their attractive size-related physico-chemical properties and biological functionality, including their high antimicrobial efficiency and non-toxic nature. Silver nanoparticles-based nanomaterials and nano-systemsare appropriate substitutions for drug delivery, wound dressing, tissue scaffold and protective coating applications. Various physicochemical parameters were related to the intrinsic antimicrobial effects exhibited by silver nanoparticles, such as size, shape, concentration, surface charge and colloidal state. Moreover, the available surface of nanosilver allows the coordination of many ligands, thus enabling remarkableoptions with respect to the surface functionalization of silver nanoparticles.

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